Research reveals how aging cells can be an underlying cause of kidney damage

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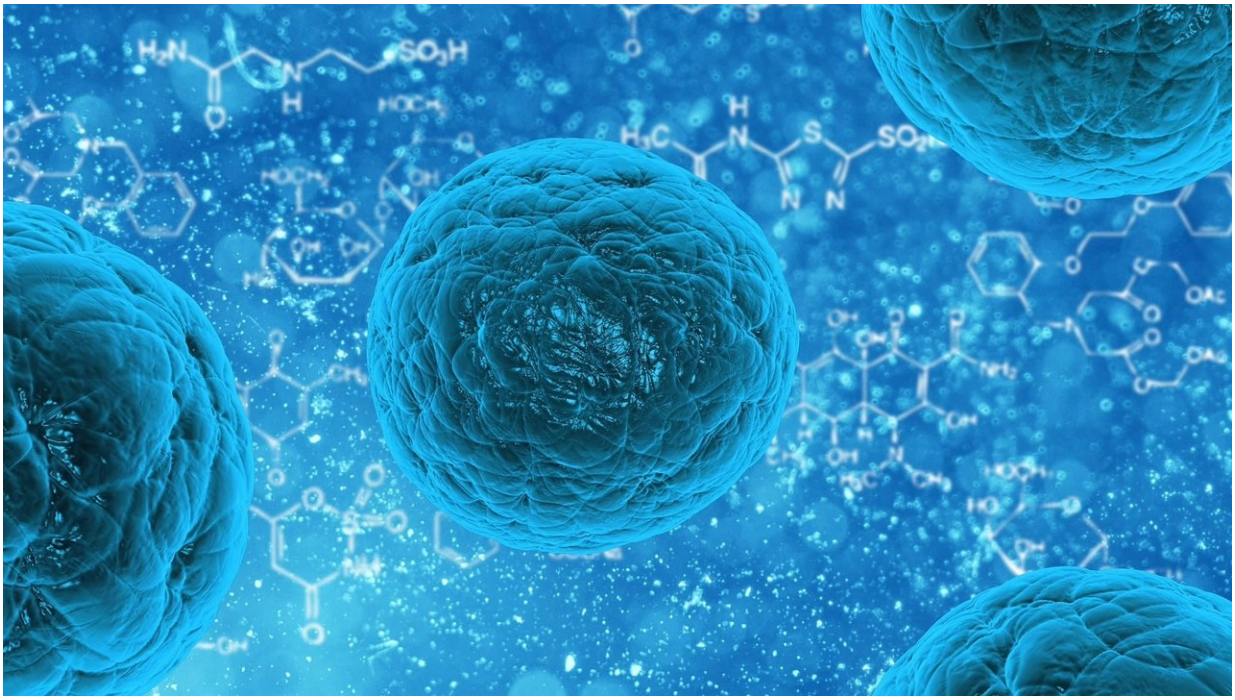

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A study in mice by researchers at Georgetown Lombardi Comprehensive Cancer Center has found that stress and tissue damage initiated by angiotensin II, a molecule that is known to increase blood pressure and stiffening in the linings of blood vessels, leads to cellular senescence, a process by which a cell ages and permanently stops dividing but does not die. Importantly, when the researchers eliminated senescent cells from

the mice, tissues returned to a normal state in spite of a continued infusion of angiotensin II.

The findings appear in *Frontiers in Cell and Developmental Biology*.

"We've known that angiotensin II can lead to hypertension and cellular damage, but our findings show that chronic, stress-induced damage due to slightly elevated blood pressure could be reduced by eliminating senescent cells," says Irfan Khan, an MD/Ph.D. candidate in the Tumor Biology program at Georgetown University and first author. "By preventing the harmful effects of angiotensin II, we revealed a novel mechanism for eliminating senescent cells that could potentially be used to develop targeted drugs to eliminate these cells."

The researchers chose angiotensin II as the tool to best induce chronic stress because they could regulate its administration and induce a measured stress level similar to that seen in people who see a slow rise in blood pressure over a lifetime. This stress typically results in less flexibility in the lining of blood vessels, which in turn leads to higher blood pressure. The researchers discovered that these effects are particularly pronounced in the kidneys and not in the brain or lungs, which is what they expected when they started their experiments.

"We can give people angiotensin lowering drugs to treat their high blood pressure. But they have to be given continuously for a lifetime and may need to be combined with other drugs to improve their efficacy. There is a pressing need to address the serious systemic effects of high blood pressure and come up with novel treatments to avoid or reverse damage to the kidneys," says Anton Wellstein, MD, Ph.D., professor of oncology and pharmacology at Georgetown Lombardi and corresponding author for this article. "Essentially, we're building the biological basis for a new therapeutic approach to address the senescence aspect of disease that has mostly been unexplored and untreated. Eliminating senescent cells with a

tolerable, short-term therapy could potentially alleviate chronic cardiovascular disease and reduce the need for a lifetime of therapy."

The researchers don't think anti-senescence drugs are going to be the fountain of youth, but they hope to be able to reverse some premature tissue damage. "A senescence drug would probably be a very short-term treatment, maybe just a few days to two weeks," Wellstein says. "Rather than constantly trying to dampen down high blood pressure, we propose getting rid of the senescent cells so that a physician could more easily treat the primary causes."

More information: Irfan Khan et al, Low Dose Chronic Angiotensin II Induces Selective Senescence of Kidney Endothelial Cells, *Frontiers in Cell and Developmental Biology* (2021). DOI: 10.3389/fcell.2021.782841

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